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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/385,918	08/30/99	HOEKSTRA M	860098.433

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EXAMINER	
ANDRES, J	
ART UNIT	**PAPER NUMBER**
1642	6

DATE MAILED: 05/23/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/385,918	HOEKSTRA ET AL.	
	Examiner	Art Unit	
	Janet L Andres	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-54 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claims 1-54 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of the CERTIFIED copies of the priority documents have been:

1.☐ received.

2.☐ received in Application No. (Series Code / Serial Number) _____ .

3.☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

14) ☐ Notice of References Cited (PTO-892)
15) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
16) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
17) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
18) ☐ Notice of Informal Patent Application (PTO-152)
19) ☐ Other:

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-10, drawn to methods of screening for modulators of ubiquitin ligase/SMAD binding, classified in class 435, subclass 7.21.

II. Claims 11-15, drawn to methods of screening for modulators of SMAD ubiquitination in lysates, classified in class 435, subclass 7.21

III. Claims 16-20 and, drawn to methods of screening for modulators of SMAD levels through stimulation of cells with BMP, classified in class 435, subclass 7.21.

IV. Claims 21-25, drawn to methods of screening for modulators of SMAD ubiquitination through stimulation of cells with BMP, classified in class 435, subclass 7.21.

V. Claims 26-28, drawn to methods of screening for modulators of SMAD levels through stimulation of cells with TGF beta, classified in class 435, sublclass 7.21.

VI. Claims 29-31, drawn to methods of screening for modulators of SMAD ubiquitination through stimulation of cells with TGF beta, classified in class 435, subclass 7.21.

VII. Claims 32-35, drawn to methods of screening for modulators of ubiquitin ligase activity by stimulation of cells with BMP, classified in class 435, subclass 7.21.

VIII. Claims 36 and 37, drawn to methods of screening for modulators of ubiquitin ligase activity by stimulation of cells with TGF beta, classified in class 435, subclass 7.21.

IX. Claims 38-40, 44, 45, 48-50, and 54, drawn to methods of inhibiting ubiquitin ligase/SMAD binding, classified in class 435, subclass 183.

X. Claims 41-43, 46, 47, and 54, drawn to methods of inhibiting SMAD ubiquitination, classified in class 435, subclass 183.

The inventions are distinct, each from the other because of the following reasons:

The invention of Group I is distinct from the invention of Group II because, while affecting the ability of SMAD to bind to ubiquitin ligase will affect SMAD ubiqutination, SMAD ubiquitination can also be modulated in other ways, such as by inhibition of ubiquitin ligase activity.

The invention of Group I is distinct from the invention of Group III because alterations in SMAD levels can occur by pathways distinct from binding to ubiquitin ligase, such as changes in protein synthesis.

The invention of Group I is distinct from the invention of IV because, while affecting the ability of SMAD to bind to ubiquitin ligase will affect SMAD ubiqutination, SMAD

ubiquitination can also be modulated in other ways, such as by inhibition of ubiquitin ligase activity.

The invention of Group I is distinct from the invention of V because alterations in SMAD levels can occur by pathways distinct from binding to ubiquitin ligase, such as changes in protein synthesis.

The invention of Group I is distinct from the invention of VI because, while affecting the ability of SMAD to bind to ubiquitin ligase will affect SMAD ubiqutination, SMAD ubiquitination can also be modulated in other ways, such as by inhibition of ubiquitin ligase activity.

The invention of Group I is distinct from the invention of Group VII because the ubiquitin ligase can ubiquitinate proteins other than SMADs; factors identified by the invention of Group I would not necessarily be the same as those identified by the invention of Group VII.

The invention of Group I is distinct from the invention of VIII because the ubiquitin ligase can ubiquitinate proteins other than SMADs; factors identified by the invention of Group I would not necessarily be the same as those identified by the invention of Group VII.

The invention of Group I is distinct from the invention of Group IX because the invention of Group I is a screen for a molecule and the invention of Group IX is a method of using said molecule. Molecules identified by other methods, such as by effects on ubiquitin ligase activity, could be used in the invention of Group IX.

The invention of Group I is distinct from the invention of Group X because molecules identified by other methods, such as by effects on ubiquitin ligase activity, could be used in the invention of Group X.

The invention of Group II is distinct from the invention of Group III because SMAD levels could be affected in other ways than by ubiquitination and proteolysis, such as effects on protein synthesis, and the molecules identified by the screen of Group II would not necessarily be the same as the molecules identified by the screen of Group III.

The invention of Group II is distinct from the invention of Group IV because the invention of Group II is drawn to a method involving a cell lysate, while the method of Group IV involves a whole cell. Different products are thus required for each of these methods, and different molecules may be identified by the different methods.

The invention of Group II is distinct from the invention of Group V because SMAD levels could be affected in other ways than by ubiquitination and proteolysis, such as effects on protein synthesis, and the molecules identified by the screen of Group II would not necessarily be the same as the molecules identified by the screen of Group V.

The invention of Group II is distinct from the invention of Group VI because the invention of Group II is drawn to a method involving a cell lysate, while the method of Group VI involves a whole cell. Different products are thus required for each of these methods, and different molecules may be identified by the different methods.

The invention of Group II is distinct from the invention of Group VII because SMAD ubiquitination could be affected by factors other than those affecting ubiqutin ligase activity, such as inhibitors of ubiquitin ligase/SMAD binding.

The invention of Group II is distinct from the invention of Group VIII because SMAD ubiquitination could be affected by factors other than those affecting ubiqutin ligase activity, such as inhibitors of ubiquitin ligase/SMAD binding.

The invention of Group II is distinct from the invention of Group IX because molecules identified by other methods, such as by effects on ubiquitin ligase activity, could be used in the invention of Group IX.

The invention of Group II is distinct from the invention of Group X because molecules identified by other methods, such as by effects on ubiquitin ligase activity, could be used in the invention of Group X.

The invention of Group III is distinct from the invention of Group IV because SMAD levels could be affected in other ways than by ubiquitination and proteolysis, such as effects on protein synthesis, and the molecules identified by the screen of Group IV would not necessarily be the same as the molecules identified by the screen of Group III.

The invention of Group III is distinct from the invention of Group V because the invention of Group III involves stimulation by BMP, while the invention of Group V involves stimulation by TGF beta. These are different molecules with different pathways, different reagents are required and the molecules identified by the invention

of Group III would not necessarily be the same as the molecules identified by the invention of Group V.

The invention of Group III is distinct from the invention of Group VI because SMAD levels could be affected in other ways than by ubiquitination and proteolysis, such as effects on protein synthesis, and the molecules identified by the screen of Group IV would not necessarily be the same as the molecules identified by the screen of Group III.

The invention of Group III is distinct from the invention of Group VII because SMAD levels can be affected by means other than ubiquitination, such as alterations in protein synthesis.

The invention of Group III is distinct from the invention of Group VIII because SMAD levels can be affected by means other than ubiquitination, such as alterations in protein synthesis.

The invention of Group III is distinct from the invention of Group IX because because molecules identified by other methods, such as by effects on ubiquitin ligase activity, could be used in the invention of Group IX.

The invention of Group III is distinct from the invention of Group X because because molecules identified by other methods, such as by effects on ubiquitin ligase activity, could be used in the invention of Group X.

The invention of Group IV is distinct from the invention of Group V because SMAD levels could be affected in other ways than by ubiquitination and proteolysis, such as

effects on protein synthesis, and the molecules identified by the screen of Group IV would not necessarily be the same as the molecules identified by the screen of Group V.

The invention of Group IV is distinct from the invention of Group VI because the invention of Group IV involves stimulation of cells by BMP, while the invention of Group VI involves stimulation by TGF beta. These are different molecules with different pathways, different reagents are required and the molecules identified by the invention of Group IV would not necessarily be the same as the molecules identified by the invention of Group VI.

The invention of Group IV is distinct from the invention of Group VII because SMAD ubiquitination could be affected by factors other than those affecting ubiqutin ligase activity, such as inhibitors of ubiquitin ligase/SMAD binding.

The invention of Group IV is distinct from the invention of Group VIII because SMAD ubiquitination could be affected by factors other than those affecting ubiqutin ligase activity, such as inhibitors of ubiquitin ligase/SMAD binding.

The invention of Group IV is distinct from the invention of Group IX because molecules identified by other methods, such as by effects on ubiquitin ligase activity, could be used in the invention of Group IX.

The invention of Group IV is distinct from the invention of Group X because molecules identified by other methods, such as by effects on ubiquitin ligase activity, could be used in the invention of Group X.

The invention of Group V is distinct from the invention of Group VI because SMAD levels could be affected in other ways than by ubiquitination and proteolysis, such as effects on protein synthesis, and the molecules identified by the screen of Group VI would not necessarily be the same as the molecules identified by the screen of Group V.

The invention of Group V is distinct from the invention of Group VII because SMAD levels can be affected by means other than ubiquitination, such as alterations in protein synthesis.

The invention of Group V is distinct from the invention of Group VIII because SMAD levels can be affected by means other than ubiquitination, such as alterations in protein synthesis.

The invention of Group V is distinct from the invention of Group IX because because molecules identified by other methods, such as by effects on ubiquitin ligase activity, could be used in the invention of Group IX.

The invention of Group V is distinct from the invention of Group X because because molecules identified by other methods, such as by effects on ubiquitin ligase activity, could be used in the invention of Group X.

The invention of Group VI is distinct from the invention of Group VII because SMAD ubiquitination could be affected by factors other than those affecting ubiqutin ligase activity, such as inhibitors of ubiquitin ligase/SMAD binding.

The invention of Group VI is distinct from the invention of Group VIII because SMAD ubiquitination could be affected by factors other than those affecting ubiqutin ligase activity, such as inhibitors of ubiquitin ligase/SMAD binding.

The invention of Group VI is distinct from the invention of Group IX because molecules identified by other methods, such as by effects on ubiquitin ligase activity, could be used in the invention of Group IX.

The invention of Group VI is distinct from the invention of Group X because molecules identified by other methods, such as by effects on ubiquitin ligase activity, could be used in the invention of Group X.

The invention of Group VII is distinct from the invention of Group VIII because the invention of Group VII involves stimulation of cells by BMP, while the invention of Group VIII involves stimulation by TGF beta. These are different molecules with different pathways, different reagents are required and the molecules identified by the invention of Group VII would not necessarily be the same as the molecules identified by the invention of Group VIII.

The invention of Group VII is distinct from the invention of Group IX because the invention of Group VII is a screen for a molecule and the invention of Group IX is a method of using said molecule. Molecules identified by the methods of Group VII would not necessarily be useful in the method of Group IX, and molecules identified by other methods, such as by direct assay in lysates, could be used in the invention of Group IX.

The invention of Group VII is distinct from the invention of Group X because the invention of Group VII is a screen for a molecule and the invention of Group X is a method of using said molecule. Molecules identified by the methods of Group VII would not necessarily be useful in the method of Group X, and molecules identified by other methods, such as by direct assay in lysates, could be used in the invention of Group X.

The invention of Group VIII is distinct from the invention of Group IX because the invention of Group VIII is a screen for a molecule and the invention of Group IX is a method of using said molecule. Molecules identified by the methods of Group VIII would not necessarily be useful in the method of Group IX, and molecules identified by other methods, such as by direct assay in lysates, could be used in the invention of Group IX.

The invention of Group VIII is distinct from the invention of Group X because the invention of Group VIII is a screen for a molecule and the invention of Group X is a method of using said molecule. Molecules identified by the methods of Group VIII would not necessarily be useful in the method of Group X, and molecules identified by other methods, such as by direct assay in lysates, could be used in the invention of Group X.

The invention of Group IX is distinct from the invention of Group X because, while inhibition of SMAD/ubiquitin ligase binding would inhibit SMAD ubiquitination, SMAD ubiquitination could also be affected by other factors, such as inhibition of ubiquitin ligase activity.

Because these inventions are distinct for the reasons given above and the search required for each group is not required for other groups, restriction for examination purposes as indicated is proper.

2. This application contains claims directed to the following patentably distinct species of the claimed invention:

Species A. Factors affecting the TGF-beta/SMAD 2/SMAD 3 pathway.

Species B. Factors affecting the BMP/SMAD1/SMAD5 pathway.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 1-19, 38-41, 44-46, 48-51, and 54 are generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet Andres, Ph.D., whose telephone number is (703) 305-0557. The examiner can normally be reached on Monday through Friday from 8:00 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D., can be reached at (703) 308-3995. The fax phone number for this Group is (703) 305-3014 or (703) 308-4242.

Communications via internet email regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [**anthony.caputa@uspto.gov**].

All Internet email communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35

U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark Office on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Janet L. Andres, Ph.D.
May 19, 2000

Yvonne Eyler

YVONNE EYLER, PH.D
PRIMARY EXAMINER